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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/021,509
Filing Date: December 07, 2001
Appellant(s): GINGRAS ET AL.

Daniel Pereira
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 09/21/06 appealing from the Office action mailed 08/24/06.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is incorrect. A correct statement of the status of the claims is as follows: Claims 1, 3, 5, 11, 15, 16 and 40-42 are active and rejected.

On page 1 of the Appeal Brief, Appellant asserts that claim 42 was indicated as being withdrawn in the Office Action, mailed on October 21, 2005.

It is noted however, that in the Office Action mailed on 08/24/06 it has been explicitly stated that " claim 42 was inadvertently omitted from the rejections under 35 U.S.C. 112 first paragraph and under 35 U.S.C. 102(e) in the Office Action, mailed on 10/21/2005".

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct.

However, it is noted that on page 4 of the Brief, Appellant indicated that:

A. Claims 1,3, 5, 11, 16 and 40-42 have been rejected under 35 U.S.C. 112, first paragraph enablement rejection.

B. Claims 1,3,5,11,15,16,40 and 41 have been rejected under 35 U.S.C. 112, first paragraph, new matter rejection.

Contrary to Appellant's statement, the following claims have been rejected:

A. Claims 1, 3, 5, 11, 15 , 16 and 40-42 have been rejected under 35 U.S.C. 112, first paragraph enablement rejection.

B. Claims 1, 3, 5, 11, 15; 16 and 40 –42 have been rejected under 35 U.S.C. 112, first paragraph, new matter rejection.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

US Patent 6,420,526 RUBEN et al., July 16, 2002.

US Patent 6, 504,010 WANG et al, January 7, 2003.

Feldman et al ., Transplant. Proc. 1998, 30, 4126-4127.

Cochlovius et al., Modern Drug Discovery, 2003, pages 33-38.

Van Noort et al., International Review of Cytology, 1998, v.178, pages 127-204.

Mikayama et al., PNAS, 1993. 90: 10056-10060.

Burgess et al ., J Cell Biol. 111:2129-2138, 1990.

Lazar et al. Mol Cell Biol. 8:1247-1252, 1988.

Ngo et al, The Protein Folding Problem and Tertiary Structure Prediction, 1994. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Issue I, Enablement rejection under 35 U.S.C. 112, first paragraph

Claims 1, 3, 5, 11, 15, 16 and 40-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the limitted working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The specification only discloses: (i) the levels of TREM-1 expression in various tissues and cell types (see Examples 4 and 5 in particular); (ii) the levels of TREM-1 splice variant, in samples collected from normal individuals and individual suffering from an autoimmune disease (see example 10 in particular); (iii) *in vitro* data indicating that TREM-1 splice variant, a polypeptide comprising SEQ ID NO:2 can down regulate LPS-induced cytokine production (see example 11 in particular); (iv) a competitive inhibitor for the ligand of TREM-1, wherein said competitive

inhibitor is a polypeptide comprising SEQ ID NO:2 (see page 14 in particular). The specification does not adequately teach how effectively modulate *any* immune response in the animal, including human, by administering: (i) an effective amount of composition comprising *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof , claimed in claims 1 and 42 or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3. Moreover, no animals models were used to study the effectively to modulate *any* immune response in the animal, including human, by administering : (i) an effective amount of composition comprising *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof , claimed in claims 1 and 42 or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3. The specification only states that it is envisioned that administering of TREM-1 splice variant may resulting down regulation of the inflammatory response (see page 45 in particular).

Moreover, it is noted that that Specification define "modulating an immune response " as a capacity of either increase or decrease immune response (see page 10 of the Specification as filed). How can administering the same amount of the same composition of soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof simultaneously results in two opposite effects, i.e. either increase or decrease immune response ?

Since there is no animal model studies and data in the specification to show the effectively of the claimed method to modulate *any* immune response in the animal, including human, by administering : (i) an effective amount of composition comprising *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic

thereof , claimed in claims 1 and 42 or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3, it is unpredictable how to correlate *in vitro* results with *in vivo* use. Bouchon et al., (IDS) teaches that distinct TREM receptors are involved in regulation of various types of immune responses including acute and chronic inflammatory responses (see entire document, page 4995 in particular). Feldman et al (Transplant. Proc. 1998, 30, 4126-4127) teach that "while it is not difficult to study the pathogenesis of animal models of disease, there are multiple constraints on analyses of the pathogenesis of human disease, leading to interesting dilemmas such as how much can we rely on and extrapolate from animal models in disease". Feldman et al., further teach that in a chronic immune-driven inflammatory response there are a number of pathways that become engaged and effective therapy in immune inflammatory diseases such as rheumatoid arthritis, will come from therapy aimed at several points in the disease pathway. In addition, Cochlovius et al (Modern Drug Discovery, 2003, pages 33-38) teach that in contrast to *in vitro* models, and partly animal-human xenograft systems, tissue cells *in vivo* seems to express molecules for defense against cellular immune systems as well as against complement. Although these defense mechanisms are still poorly understood, they provide some hints as to why many potential therapeutics perform marvelously in vitro but a fairly high portion of them still fail in vivo. Since a method of modulating an immune response comprising administering: (i) an effective amount of composition comprising *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof , or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, can be species- and model-dependent (see Van Noort et al. International Review of Cytology, 1998, v.178, pages 127-204, Table III in particular) , it is not clear that reliance on the *in vitro* studies accurately reflects the relative mammal and human efficacy of the claimed therapeutic strategy. Van Noort et al. further indicates factors that effect immune response such as genetic, environmental and hormonal (Page 176, Paragraph 3).

The ability of a host to enhance an immune response will vary depending upon factors such as the condition of the host and burden of disease. The specification does not teach how to extrapolate data obtained from *in vitro* studies to the development of effective method of modulating an immune response in any animal, including human commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of a method of modulate *any* immune response in the animal, including human, by administering (i) an effective amount of composition comprising *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, claimed in claims 1 and 42 or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3. Thus in the absence of working examples or detailed guidance in the specification, the intended *in vivo* uses of (i) *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or (ii) any polypeptide mimetic thereof or (ii) *any* soluble polypeptide wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2 to modulate an immune response in any animal including human are fraught with uncertainties.

It addition, an effective method to modulate an immune response in any animal including human, comprising administering: (i) an effective amount of composition comprising *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, in the absence of *in vivo* data are unpredictable for the following reasons: (1) the polypeptide may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the polypeptide may not reach the target area because, it may not be able to cross the mucosa or the polypetide may be adsorbed by fluids, cells and tissues where the

polypetide has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Also an issue that Appellant has not taught how to make a composition comprising *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2 to effectively modulate an immune response in any animal, including human. The structural and functional characteristics of said *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof or wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2 are not defined in the specification or claims.

The terms " with" or "has" are considered to be an open-ended claim language and includes amino acid residues outside of the specified peptide. Therefore, a polypeptide " with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof", claimed in claim 1; or polypeptide that has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3 includes an unlimited number of amino acid sequences.

The disclosure of a specific TREM-1 splice variant, a polypeptide of SEQ ID NO:2, that has been shown *in vitro* to down regulate LPS-induced cytokine production , cannot support the entire genus of peptides comprising at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2, the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino

acids 36-114 of SEQ ID NO:2 as part of their sequence that can be used to modulate an immune response in any animal, including human .

Appellant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated *any* polypeptide: (i) with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, claimed in claim 1; or (ii) that has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3, encompassed by the claimed invention other than "a polypeptide consisting of the amino acid sequence of SEQ ID NO: 2" would be expected to have greater differences in their activities.

T he specification fails to provide sufficient guidance as to which core structure of SEQ ID NOs: 2 is essential to modulate an immune response and which changes can be made in the structure of SEQ ID No 2 and still maintained the same function. There is insufficient direction or objective evidence in the Specification as to how to make a polypeptide: (i) with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, claimed in claim 1; or (ii) that has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3 that can be used for modulating an immune response. While any polypeptide "(i) with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, claimed in claim 1; or (ii) that has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3" may have some notion of the activity of the " a polypeptide consisting the amino acid sequence of SEQ ID NO.2", claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make such agents, commensurate in scope with the claimed invention.

Since the instant fact pattern fails to indicate that representative number of structurally related compounds is disclosed, the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claims and consequently would not know how to make them. An assay for *finding* a product is not equivalent to a positive recitation of *how to make* a product.

Protein chemistry is probably one of the most unpredictable areas of biotechnology . It is known in the art that even single amino acid changes or differences in a proteins amino acid sequence can have dramatic effects on the protein's function. For example, Mikayama et al. (PNAS, 1993. 90: 10056-10060) teach that the human glycosylation factor (GIF) protein differs from human macrophage migration inhibitory factor (MIF) by a single amino acid residue (see Figure 1 in particular). Yet, Mikayama et al. further teach that GIF is unable to carry out the function of MIF and MIF does not demonstrate GIF activity (see Abstract in particular). Burgess et al (J Cell Biol. 111:2129-2138, 1990) show that a conservative replacement of a single "lysine" reside at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein. Similarly, Lazar et al. (Mol Cell Biol. 8:1247-1252, 1988) teach that in transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagines did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen. These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed polypeptide of SEQ ID NO:2 can be tolerated that will allow said polypeptide to function as claimed, i.e. to modulate an immune response. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions.

Since the amino acid sequence of a polypeptide determines its structure and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. modulate an immune response) requires a knowledge of, and guidance with regard to, which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification) and detailed knowledge of the ways in which a polypeptide's structure relates to it's functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single amino acid sequence and in turn utilizing predicted structural determinations to ascertain functional aspects the peptides and finally, what changes can be tolerated with respect thereto is complex and well outside the realm of routing experimentation. Because of the lack of sufficient guidance and predictability in determining which structures would lead to functional proteins or peptides with the desired properties and that the relationship between the sequence of a peptide and it's tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al, in The Protein Folding Problem and Tertiary Structure Prediction, 1994. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.); it would require an undue amount of experimentation for one of skill in the art to arrive at the breadth of proteins encompassed by the claimed invention. Without sufficient guidance, the changes which can be made in the structure of any polypeptide (i) with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, claimed in claim 1; or (ii) that has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3 and still be able to be a competitive inhibitor of the ligand for TREM-1 is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

Thus, Appellant has not provided sufficient guidance to enable one skill in the art to use claimed method of modulate *any* immune response in the animal, including human, by administering: (i) an effective amount of composition comprising *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, claimed in

claims 1 and 42 or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3 in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Issue II Rejection under 35 U.S.C. 102 (e)

Claims 1,3,5,11, 15,16 and 40-42 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,420,526 or US Patent 6,504,010.

US Patent '526 teaches a method of modulation an immune response in a subject suffering from disease comprising administering a polypeptide of SEQ ID NO: 478 in a pharmaceutical carrier (see entire document , abstract, columns 4, 8 ,77 in particular). It is noted that SEQ ID : 2 of the instant application is 100 % identical to SEQ ID NO: 478 of US Patent '526 (see attached sequence alignment) . US Patent '526 teaches that disease are infectious disease, GVHD and septic shock (see column 77 and 132 in particular). Although the reference is silent about decreasing the activity of DAP12/TREM1 complex after administering of SEQ ID NO: 478, or that SEQ ID NO: 478 is a competitive inhibitor of the ligand to TREM-1 these functional limitations would be inherent properties of said polypeptide because it is 100 % identical with the claimed SEQ ID NO:2. Since the office does not have a laboratory to test the

reference polypeptide, it is Appellant's burden to show that the reference polypeptide does not decrease the activity of DAP12/TREM1 complex or not a competitive inhibitor of the ligand to TREM-1 as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

Claims 15, 16 and 40-42 are included because the claimed functional limitation would be inherent properties of the a method of modulation an immune response and a method of modulation an inflammatory response in a subject suffering from disease comprising administering a polypeptide of SEQ ID NO: 478 taught by US Patent '526 because the referenced polypeptide of SEQ ID : 478 used in the referenced methods is 100 % identical with the claimed SEQ ID NO:2 used in the claimed methods. It is clear that US Patent '526 and the current application administered the same compound to achieved the same results in the same patients thus the reference polypeptide would inherently performed the intended use. If the prior art structure is capable of performing the intended use, then it meets the claim. When a claim recites using an old composition or structure (e.g. polypeptide of SEQ ID NO: 478) and the use is directed to a result or property of that composition or structure then the claim is anticipated. In addition, under the principles of inherency, if a prior art method, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art. When the prior art method is the same as a method described in the specification, it can be assumed the method will inherently perform the claimed process. See MPEP 2112.02 . Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Similarly, US Patent '010 teaches a method of modulation an immune response in a subject suffering from disease comprising administering a polypeptide of SEQ ID NO: 1825 in a pharmaceutical carrier (see entire document , abstract, column3 45, 46, 78 and 79 in particular). It is noted that SEQ ID :2 of the instant application is 100 % identical to SEQ ID

NO: 1825 of US Patent '010 (see attached sequence alignment). Although the reference is silent about decreasing the activity of DAP12/TREM1 complex after administering of SEQ ID NO: 1825, or that SEQ ID NO: 1825 is a competitive inhibitor of the ligand to TREM-1 these functional limitations would be inherent properties of said polypeptide because it is 100 % identical with the claimed SEQ ID NO:2. Since the office does not have a laboratory to test the reference polypeptide, it is Appellant's burden to show that the reference polypeptide does not decrease the activity of DAP12/TREM1 complex or not a competitive inhibitor of the ligand to TREM-1 as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

Claims 15,16 and 40-42 are included because the claimed functional limitation would be inherent properties of the a method of modulation an immune response and a method of modulation an inflammatory response in a subject suffering from disease comprising administering a polypeptide of SEQ ID NO: 1825 taught by US Patent '010 because the referenced polypeptide of SEQ ID : 010 used in the referenced methods is 100 % identical with the claimed SEQ ID NO:2 used in the claimed methods. It is clear that US Patent '010 and the current application administered the same compound to achieved the same results in the same patients thus the reference polypeptide would inherently performed the intended use. If the prior art structure is capable of performing the intended use, then it meets the claim. When a claim recites using an old composition or structure (e.g. polypeptide of SEQ ID NO: 1825) and the use is directed to a result or property of that composition or structure then the claim is anticipated. In addition, under the principles of inherency, if a prior art method, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art. When the prior art method is the same as a method described in the specification, it can be assumed the method will inherently perform the claimed process. See MPEP 2112.02 . Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

The reference teaching anticipates the claimed invention.

Issue III. Rejection under 35 U.S.C. 112, first paragraph, New Matter rejection.

Claims 1, 3, 5, 11, 15, 16, 40-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection.**

" composition of soluble polypeptides with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof in the amount effective to modulate the levels of TREM-1 and or TREM-1SV ligand binding activity", claimed in claim 1 or (ii) " composition comprising *any* soluble polypeptide wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2, the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2", claimed in claim 3, represent a departure from the specification and the claims as originally filed. The passages pointed by the Appellant do not provide a clear support for " composition of soluble polypeptides with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof in the amount effective to modulate the levels of TREM-1 and or TREM-1SV ligand binding activity", claimed in claim 1 or (ii) " composition comprising *any* soluble polypeptide wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2, the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2", claimed in claim 3.

The specification and the claims as originally field only support a general recitation of polypeptide spliced variant of TREM-1 of SEQ ID NO:2, in which several , 5 to 10, 1 to 5 1 to 3,2, 1 or no amino acid residues are substituted, deleted or added.

(10) Response to Argument

Issue I, Enablement rejection under 35 U.S.C. 112, first paragraph

Claims 1, 3, 5, 11, 15 , 16 and 40-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

At page 6 of the Brief, Appellant asserts that while there is no working examples in the specification, there is sufficient guidance in the specification that provide the necessary knowledge for using the claimed method . Appelant further assertsd that one can practice the claimed invention because one can predict the therapeutical efficacy of the composition with TREM-1 ligand activity, since the mechanisms by which the polypeptide competes for the TREM-1 ligand is described throughout the specification;

At page 7 of the Brief, Appelant asserts that the structure of different TREM-1 molecules across species have been studied and their ligand binding site is a common conservative region, as supported by the teaching og Kelker et al. Although Kelker et al., **could not identify the exact sequence of the binding site in the loop domain as pointed by the Examiner**, the work of Kelker et al., has confirmed the structure and presence of these loops domains in the different TREM-1 molecules studied.

At page 8 of the Brief, Appelant asserts that Bouchon et al (Nature ,2001, 410 1103-1107) reference utilized the teaching of the present invention, thus showing the enablement of the present invention.

At page 9 of the Brief, Appelant asserts that the Examiner is requiring human trials as the only sufficient support for what te Examiner perceivesis enablement of the claims.

Contrary to Appellant assertion, the issue raised by the Examiner was not about the proposed mechanism of action of soluble polypeptide variant of TREM. As has been stated supra, the specification only discloses: (i) the levels of TREM-1 expression in various tissues and cell types (see Examples 4 and 5 in particular); (ii) the levels of TREM-1 splice variant, in samples collected from normal individuals and individual suffering from an autoimmune disease (see example 10 in particular); (iii) *in vitro* data indicating that TREM-1 splice variant, a polypeptide comprising SEQ ID NO:2 can down regulate LPS-induced cytokine production (see example 11 in particular); (iv) a competitive inhibitor for the ligand of TREM-1, wherein said competitive inhibitor is a polypeptide comprising SEQ ID NO:2 (see page 14 in particular). The specification does not adequately teach how effectively modulate *any* immune response in the animal, including human, by administering: (i) an effective amount of composition comprising *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, claimed in claims 1 and 42 or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3. Moreover, no animals models were used to study the effectively to modulate *any* immune response in the animal, including human, by administering : (i) an effective amount of composition comprising *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, claimed in claims 1 and 42 or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3. The specification only states that it is envisioned that administering of TREM-1 splice variant may resulting down regulation of the inflammatory response (see page 45 in particular).

Moreover, it is noted that that Specification define "modulating an immune response " as a capacity of either increase or decrease immune response (see page 10 of the Specification as filed). How can administering the same amount of the same composition of soluble

polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof simultaneously results in two opposite effects, i.e. either increase or decrease immune response ?

With regards to the issue that the Examiner is requiring human trials as the only sufficient support for what te Examiner perceivesis enablement of the claims.

The examiner does not require any human trials as asserted by Appellant. However, the Examiner stated that since there is no animal model studies and any *in vivo* data in the specification to show the effectively of the claimed method to modulate *any* immune response in the animal, including human, by administering : (i) an effective amount of composition comprising *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof , claimed in claims 1 and 42 or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3, it is unpredictable how to correlate *in vitro* results with *in vivo* use. Therefore, it is the Examiner position that it is not clear that the skilled artisan could predict the efficacy of a method to modulate *any* immune response in the animal, including human, by administering : (i) an effective amount of composition comprising *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof , claimed in claims 1 and 42 or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3. Thus in the absence of working examples or detailed guidance in the specification, the intended *in vivo* uses of composition comprising *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof , claimed in claims 1 and 42 or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID

NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3 to modulate any immune response are fraught with uncertainties.

With regards to the issue that Bouchon et al., (Nature ,2001, 410 1103-1107) reference utilized the teaching of the present invention, thus showing the enablement of the present invention.

Bouchon et al., (Nature ,2001, 410 1103-1107) reference only teaches a very specific mTREM-1/IgG1 fusion protein, that was used in experimental endotoxic shock on murine models. However, Bouchon et al., explicitly stressed that experimental endotoxic shock reproduced human sepsis only in part as it does not involve the replication and dissemination of bacteria (see page 1105 in particular). The is no teaching or suggestion in Bouchon et al. to: (i) effectively modulate *any* immune response in animals including human by administering an effective amount of composition comprising : (i) *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof , claimed in claims 1 and 42 or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3.

With regards to Appellant's comments that the structure of different TREM-1 molecules across species have been studied and their ligand binding site is a common conservative region, as supported by Kelker et al.

It is noted , Kelker et al., explicitly stated that " the structural data presented here do not unfortunately allow for very informed speculation on precise ligand binding sites or on potential ligand (see page 1180 in particular).

The issue raised by the Examiner was not about the presence of loops domains in the different TREM-1 molecules studied. Appellant himself acknowledge that Kelker et al., **could not**

identify the exact sequence of the binding site in the loop domain (see page 7 of the Appel Brief filed on 09/21/06). However, the presence of that specific sequences in the soluble splice variants of TREM-1 are essential for the ability of said soluble splice variants of TREM-1 to be a competitive inhibitors of the ligand for TREM-1, and thus to be used in the claimed method of modulating an immune response (see ovelapping pages 4 and 5 of the Instant Specification).

As has been stated supra, Appellant has not taught how to make a composition comprising *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof , or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2 to effectively modulate an immune response in any animal, including human. The structural characteristics of said *any* soluble polypeptide with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof or wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2 that are essential to maintain the asserted function, i.e. to modulate an immune response are not defined in the specification or claims.

The terms " with" or "has" are considered to be an open-ended claim language and includes amino acid residues outside of the specified peptide. Therefore, a polypeptide " with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof ", claimed in claim 1; or polypeptide that has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3 includes an unlimited number of amino acid sequences. The disclosure of a specific TREM-1 splice variant, a polypeptide of SEQ ID NO:2, that has been shown *in vitro* to down regulate LPS-induced cytokine production , cannot support the entire genus of peptides comprising at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or wherein said polypeptide has at least a portion of amino acid 36 to 114 of

SEQ ID NO:2, the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2 as part of their sequence that can be used in the method of modulating an immune response in any animal, including human .

Appellant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated *any* polypeptide: (i) with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, claimed in claim 1; or (ii) that has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3, encompassed by the claimed invention other than "a polypeptide consisting of the amino acid sequence of SEQ ID NO: 2" would be expected to have greater differences in their activities.

The specification fails to provide sufficient guidance as to which core structure sequence of SEQ ID NOs: 2 is essential for the ability of said soluble splice variants of TREM-1 to be a competitive inhibitors of the ligand for TREM-1, and thus to be used in the claimed method of modulating an immune response and which changes can be made in the structure of SEQ ID No 2 and still maintained the same function. There is insufficient direction or objective evidence in the Specification as to how to make a polypeptide: (i) with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, claimed in claim 1; or (ii) that has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3 that can be used for modulating an immune response. While any polypeptide "(i) with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, claimed in claim 1; or (ii) that has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3" may have some notion of the activity of the " a polypeptide consisting the amino acid sequence of SEQ ID

NO.2", claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make such agents, commensurate in scope with the claimed invention. The specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed polypeptide of SEQ ID NO:2 can be tolerated that will allow said polypeptide to function as claimed, i.e. to modulate an immune response. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions. Without sufficient guidance, the changes which can be made in the structure of any polypeptide (i) with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, claimed in claim 1; or (ii) that has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3" and still be able to be a competitive inhibitor of the ligand for TREM-1 is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Since the instant fact pattern fails to indicate that representative number of structurally related compounds is disclosed, the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claims and consequently would not know how to make them. An assay for *finding* a product is not equivalent to a positive recitation of *how to make* a product.

Thus, Appellant has not provided sufficient guidance to enable one skill in the art to use claimed method of modulate *any* immune response in the animal, including human, by administering: (i) an effective amount of composition comprising *any* soluble polypeptide with at least a

portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof, claimed in claims 1 and 42 or (ii) an effective amount of composition comprising *any* soluble polypeptide, wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2 the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2, claimed in claim 3 in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Issue II Rejection under 35 U.S.C. 102 (e)

Claims 1, 3, 5, 11, 15,1 6 and 40-42 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,420,526 or US Patent 6,504,010.

At page 11 of the Brief, Appellant asserts that US Patent '010 describes only hypothetical therapeutic method to treat lung cancer. The mechanism of action is unclear and no proof or evidence of such therapy using SEQ ID NO:1825 is present. There is a proposed targeted mechanism of T cell activation but thre is no scientific logic to support it.

At page 12 of the Brief, Appellant asserts that US Patent '526 is very vague patent. The '526 Patent describes a sequence with no details in the Specification on which sequence of the molecule has a function. The description in Us Patent '526 suggests a potential use to regulate the immune response but does not describe enough to practice without undue experimentation, such as which part of the molecule is relevant to practice the invention.

Appellant is relying upon an asserted and claimed mechanism of action but does not provide objective evidence that the prior art teaching of administering of polypeptide that is identical to the claimed polypeptide comprising SEQ ID NO:2 to achieve the same therapeutic effect differs from the claimed methods. Moreover, it is noted that Appellant's arguments to support his enablement rejection of the prior art references are essentially same as have been used by the Examiner for the instant case. However, it has been well settled that Section 112 (1) "provides that the specification must enable one skill in the art to 'use" the invention, whereas section 102 makes no such requirement as to an anticipatory disclosure" Hafner, 410 F.2d at 1405; see 1 Donald S. Chisum, Chisum on Patents 3.04[1][c](2002). "Even if a reference discloses an inoperative device, it is prior art for all that it teaches". Beckman Instruments v LKB Produkter AB, 892 F.2d 1547,1551,13 USPQ2d 1301,1304 (Fed.Cir. 1989).

The sequence alignment, shown that polypeptide comprising SEQ ID NO:2 of the instant application is 100 % identical to SEQ ID NO: 478 of US Patent '526 or 100 % identical to SEQ ID NO: 1825 of US Patent '010. It is noted that the terms "has" or "with" are open-ended term. It means that a peptide may include additional unrecited amino acids on either or both of the N- or C- termini of given sequence and thus can read on the recited polypeptide. Moreover, US Patent'526 teaches that polypeptides of the invention comprises the extracellular domain alone or fused to the intracellular domain i.e. lacking the transmembrane domain, i.e soluble polypeptide (see column 145, lines 1-10 in particular). Similarly, US Patent ' 010 teaches that in certain embodiments the peptides of the invention may include peptides in which

an N-terminal leader sequence and/or transmembrane domain have been deleted (see column 45, lines 55-65 in particular).

It is the Examiner position that US Patent '526 teaches a method of modulating an immune responses, i.e. decreasing an inflammatory response in a subject suffering from disease comprising administering a polypeptide of SEQ ID NO: 478 in a pharmaceutical carrier (see entire document , abstract, columns 4, 8 ,77 in particular). US Patent '526 teaches that disease are infectious disease, GVHD and septic shock (see column 77 and 132 in particular). Although the reference is silent about decreasing the activity of DAP12/TREM1 complex after administering of SEQ ID NO: 478, or that SEQ ID NO: 478 is a competitive inhibitor of the ligand to TREM-1 these functional limitations would be inherent properties of said polypeptide because it is 100 % identical with the claimed polypeptide comprising SEQ ID NO:2. Since the office does not have a laboratory to test the reference polypeptide, it is applicant's burden to show that the reference polypeptide does not decrease the activity of DAP12/TREM1 complex or not a competitive inhibitor of the ligand to TREM-1 as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

Claims 11, 15, 16 and 40-42 are included because the claimed functional limitation would be inherent properties of the a method of modulation an immune response and a method of modulation an inflammatory response in a subject suffering from disease comprising administering a polypeptide of SEQ ID NO: 478 taught by US Patent '526 because the referenced polypeptide of SEQ ID : 478 used in the referenced methods is 100 % identical with the claimed polypeptide comprising SEQ ID NO:2 used in the claimed methods. It is clear that US Patent '526 and the current application administered the same compound to achieved the same results in the same patients thus the reference polypeptide would inherently performed the intended use. If the prior art structure is capable of performing the intended use, then it meets the claim. When a claim recites using an old composition or structure (e.g. polypeptide of SEQ ID NO: 478) and the use is directed to a result or property of that

composition or structure then the claim is anticipated. In addition, under the principles of inherency, if a prior art method, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art. When the prior art method is the same as a method described in the specification, it can be assumed the method will inherently perform the claimed process. See MPEP 2112.02 . Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Similarly, US Patent '010 teaches a method of therapy of an immune response in a subject suffering from disease comprising administering a polypeptide of SEQ ID NO: 1825 in a pharmaceutical carrier (see entire document , abstract, column 3, 45, 46, 78 and 79 in particular). It is noted that polypeptide compising SEQ ID :2 an of the instant application is 100 % identical to SEQ ID NO: 1825 of US Patent '010 (see attached sequence alignment). Although the reference is silent about decreasing the activity of DAP12/TREM1 complex after administering of SEQ ID NO: 1825, or that SEQ ID NO: 1825 is a competitive inhibitor of the ligand to TREM-1 these functional limitations would be inherent properties of said polypeptide because it is 100 % identical with the claimed SEQ ID NO:2. Since the office does not have a laboratory to test the reference polypeptide, it is applicant's burden to show that the reference polypeptide does not decrease the activity of DAP12/TREM1 complex or not a competitive inhibitor of the ligand to TREM-1 as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

Claims 11, 15, 16 and 40-42 are included because the claimed functional limitation would be inherent properties of the a method of modulation an immune response and a method of modulation an inflammatory response in a subject suffering from disease comprising administering a polypeptide of SEQ ID NO: 1825 taught by US Patent '010 because the referenced polypeptide of SEQ ID : 010 used in the referenced methods is 100 % identical

with the claimed SEQ ID NO:2 used in the claimed methods. It is clear that US Patent '010 and the current application administered the same compound to achieved the same results in the same patients thus the reference polypeptide would inherently performed the intended use. If the prior art structure is capable of performing the intended use, then it meets the claim. When a claim recites using an old composition or structure (e.g. polypeptide of SEQ ID NO: 1825) and the use is directed to a result or property of that composition or structure then the claim is anticipated. In addition, under the principles of inherency, if a prior art method, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art. When the prior art method is the same as a method described in the specification, it can be assumed the method will inherently perform the claimed process. See MPEP 2112.02 . Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

As pointed out supra, the mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Even though Appellant has proposed or claimed the mechanism by which a particular compound might modulate an immune response it does not appear to distinguish the prior art teaching the same or nearly the same methods to achieve the same end result. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

The reference teaching anticipates the claimed invention.

Issue III. Rejection under 35 U.S.C. 112, first paragraph, New Matter rejection.

Claims 1, 3, 5, 11, 15, 16, 40-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection.**

At page 14 of the Brief, Appellant asserts that support for the phrase "composition of soluble polypeptides with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof" or " composition comprising *any* soluble polypeptide wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2, the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2" is present in great detail in the Specification on paragraphs 55,59,60, 72,73,75,76 78 and 80.

Contrary to Appellant assertion, the passages pointed by the Appellant do not provide a clear support for subgenus of claimed " composition of soluble polypeptides with at least a portion of amino acid 1 to 136 of SEQ ID NO:2 or any polypeptide mimetic thereof in the amount effective to modulate the levels of TREM-1 and or TREM-1SV ligand binding activity", claimed in claim 1 or (ii) " composition comprising *any* soluble polypeptide wherein said polypeptide has at least a portion of amino acid 36 to 114 of SEQ ID NO:2, the whole portion of amino acid 36-114 of SEQ ID NO:2 or more than the whole portion of amino acids 36-114 of SEQ ID NO:2", claimed in claim 3.

The specification and the claims as originally field only support a genus of polypeptide spliced variant of TREM-1 of SEQ ID NO:2, in which several , 5 to 10, 1 to 5 1 to 3,2, 1 or no amino acid residues are substituted, deleted or added. See *In re Smith* 173 USPQ 679, it was ruled that a genus may not support a subgenus even though there is a disclosed species within the subgenus.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the Examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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